

Amendments to the Claims:

This listing of claims will replace all prior versions, and listings, of claims in the application:

1. (Currently amended) An immunoconjugate comprising:

- (a) an antibody;
- (b) a chemotherapeutic moiety; and
- (c) a linker comprising (i) a thiol-reactive functional group that binds to a thiol group on the antibody, and (ii) a water-solubilizing moiety, and

wherein the chemotherapeutic moiety is attached to the linker via an intracellularly-cleavable moiety that is cleavable by intracellular esterases and comprises an ester formed from the α -carboxylic acid of an amino acid, and

said thiol-reactive functional group is a maleimide or vinylsulfone which links to thiol groups of said antibody.

2-4. Canceled

5. (Withdrawn) The immunoconjugate according to claim 1, wherein the intracellularly-cleavable moiety comprises a peptide bond cleavable by intracellular enzymes.

6. (Withdrawn) The immunoconjugate according to claim 1, wherein the intracellularly-cleavable moiety comprises an ether bond, susceptible to cleavage under the acidic pH of intracellular compartments.

7. (Withdrawn) The immunoconjugate according to claim 6, wherein said ether bond is the ether bond formed between the chemotherapeutic agent and said intracellularly-cleavable moiety.

8. (Withdrawn) The immunoconjugate according to claim 7, wherein said intracellularly-cleavable moiety comprises a tetrahydropyran moiety, a tetrahydrofuran moiety or an orthoester moiety.

9-12. Canceled.

13. (Previously presented) The immunoconjugate according to claim 1, wherein said water solubilizing moiety is an aminopolycarboxylate.

14. (Previously presented) The immunoconjugate according to claim 13, wherein said aminopolycarboxylate residue is selected from the group consisting of DTPA, EDTA, TTHA, benzyl-DTPA, DOTA, benzyl-DOTA, NOTA, benzyl-NOTA, TETA, a polyethylene glycol (PEG) and a N,N'-dialkyl substituted piperazine.

15. (Original) The immunoconjugate according to claim 1, wherein said chemotherapeutic moiety is selected from the group consisting of doxorubicin (DOX), epirubicin, morpholinodoxorubicin (morpholino-DOX), cyanomorpholino-doxorubicin (cyanomorpholino-DOX), 2-pyrrolino-doxorubicin (2-PDOX), CPT, CPT-11, SN-38, topotecan, taxanes, geldanamycin, ansamycins, and epothilones.

16. (Canceled)

17. (Previously presented) The immunoconjugate according to claim 1, wherein said antibody is a monoclonal antibody (mAb).

18. (Currently amended) ~~The immunoconjugate according to claim 17, wherein said monoclonal antibody~~ An immunoconjugate comprising:

- (a) an antibody;
- (b) a chemotherapeutic moiety; and

(c) a linker comprising (i) a thiol-reactive functional group that binds to a thiol group on the antibody, and (ii) a water-solubilizing moiety,

wherein said chemotherapeutic moiety is attached to said linker via an intracellularly-cleavable moiety that is cleavable by intracellular esterases and comprises an ester formed from the α -carboxylic acid of an amino acid,

and said antibody is multivalent and/or multispecific.

19. (Previously presented) The immunoconjugate according to claim 1, wherein said antibody is a murine, chimeric, humanized, or human monoclonal antibody, and said antibody is an intact, fragment (Fab, Fab', F(ab)2, F(ab')2), or sub-fragment (single-chain constructs) form.

20. (Previously Presented) The immunoconjugate according to claim 18, wherein said antibody is a murine, chimeric, humanized, or human monoclonal antibody, and said antibody is an intact, fragment (Fab, Fab', F(ab)2, F(ab')2), or sub-fragment (single-chain constructs) form.

21. (Previously presented) The immunoconjugate according to claim 1, wherein said antibody is a monoclonal antibody that is reactive with an antigen or epitope of an antigen expressed on a cancer or malignant cell.

22. (Original) The immunoconjugate according to claim 21, wherein said cancer cell is a cell from a hematopoietic tumor, carcinoma, sarcoma, melanoma or a glial tumor.

23. (Previously presented) The immunoconjugate according to claim 1, wherein said antibody is a monoclonal antibody that binds to an antigen selected from the group consisting of a B-cell lineage antigen, a T-cell antigen, a myeloid lineage antigen and an HLA-DR antigen.

24. (Previously presented) The immunoconjugate according to claim 1, wherein said antibody is a monoclonal antibody that binds to an antigen selected from the group consisting of CD74,

CD22, epithelial glycoprotein-1, MUC1, carcinoembryonic antigen (CEA or CD66e), colon-specific antigen-p, alpha-fetoprotein, CC49 antigen, prostate-specific membrane antigen, carbonic anhydrase IX, HER-2/neu, BrE3 antigen, CD19, CD20, CD21, CD23, CD33, CD45, CD74, CD80, VEGF, EGF receptor, PIgf, MUC2, MUC3, MUC4, gangliosides, HCG, EGP-2, CD37, HLA-DR, CD30, Ia, A3, A33 antigen, Ep-CAM, KS-1, Le(y), S100, PSA, tenascin, folate receptor, Thomas-Friedreich antigens, tumor necrosis antigens, tumor angiogenesis antigens, Ga 733, IL-2, IL-6, T101, MAGE, an antigen that binds to L243, CD66a (BGP), CD66b (CGM6) CD66c (NCA), CD66d (CGM1), TAC and combinations thereof.

25. (Currently Amended) The immunoconjugate according to claim 1, wherein said antibody is selected from the group consisting of LL2, L243, MN-14, G250, J591, and CC49.

26. (Currently Amended) The immunoconjugate according to claim 1, wherein said antibody is a bispecific and/or bivalent antibody construct comprising one or more antibodies selected from the group consisting of, LL2, L243, MN-14, G250, J591, and CC49.

27. (Previously presented) The immunoconjugate according to claim 1, wherein said antibody links to at least one chemotherapeutic moiety.

28. (Previously Presented) The immunoconjugate according to claim 27, wherein said antibody links to about 7 to 12 said chemotherapeutic moieties.

29. (Previously presented) The immunoconjugate according to claim 1, wherein said linker comprises a peptide comprising a thiol-reactive moiety at its N-terminus for linkage to the antibody and one or more side chain amino groups for linkage to at least one chemotherapeutic moiety.

30. (Previously presented) The immunoconjugate according to claim 1, wherein said linker comprises a peptide comprising a functional group at the N-terminus, a water-solubilizing moiety

at the C-terminus, and one or more internal basic amino acids with side chains available for attachment to said chemotherapeutic moiety

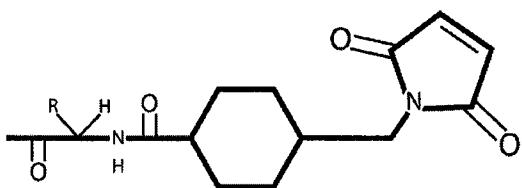
31. (Previously Presented) The immunoconjugate according to claim 30, wherein said water-solubilizing moiety is selected from the group consisting of DTPA, EDTA, TTHA, benzyl-DTPA, DOTA, benzyl-DOTA, NOTA, benzyl-NOTA, a polyethylene glycol (PEG) and N,N'-dialkyl substituted piperazine.

32. (Currently Amended) ~~The immunoconjugate of claim 1, wherein~~
An immunoconjugate comprising:

(a) an antibody;
(b) a chemotherapeutic moiety; and
(c) a linker comprising (i) a thiol-reactive functional group that binds to a thiol group on
the antibody, and (ii) a water-solubilizing moiety,

wherein said chemotherapeutic moiety is attached to said linker via an intracellularly-cleavable
moiety that is cleavable by intracellular esterases and comprises an ester formed from the α -
carboxylic acid of an amino acid,

and said linker contains an α -amino acid and is of the formula:



wherein R is an amino acid side chain, said amino acid selected from the group consisting of glycine, alanine, valine, leucine, isoleucine, proline, serine, threonine, cysteine, methionine, asparagine, glutamine, phenylalanine, tyrosine, tryptophan, lysine, arginine, histidine, aspartate and glutamate.

33. (Original) The immunoconjugate according to claim 1, wherein said immunoconjugate is in a form suitable for parenteral administration.

34. (Previously Presented) The immunoconjugate according to claim 29, wherein said chemotherapeutic moiety is selected from the group consisting of doxorubicin (DOX), epirubicin, morpholinodoxorubicin (morpholino-DOX), cyanomorpholino-doxorubicin (cyanomorpholino-DOX), 2-pyrrolino-doxorubicin (2-PDOX), CPT, CPT-11, SN-38, topotecan, taxanes, geldanamycin, ansamycins, and epothilones.

35. (Canceled)

36. (Previously Presented) The immunoconjugate according to claim 29, wherein said antibody is a monoclonal antibody (mAb).

37. (Currently Amended) ~~The immunoconjugate according to claim 36, wherein said monoclonal antibody~~

An immunoconjugate comprising:

- (a) an antibody;
- (b) a chemotherapeutic moiety; and
- (c) a linker comprising (i) a thiol-reactive functional group that binds to a thiol group on the antibody, and (ii) a water-solubilizing moiety;

wherein said chemotherapeutic moiety is attached to said linker via an intracellularly-cleavable moiety that is cleavable by intracellular esterases and comprises an ester formed from the α -carboxylic acid of an amino acid;

said linker comprises a peptide comprising a thiol-reactive moiety at its N-terminus for linkage to the antibody and one or more side chain amino groups for linkage to at least one chemotherapeutic moiety;

and said antibody is multivalent and/or multispecific.

38. (Previously Presented) The immunoconjugate according to claim 36, wherein said antibody is a murine, chimeric, humanized, or human monoclonal antibody, and said antibody is an intact, fragment (Fab, Fab', F(ab)2, F(ab')2), or sub-fragment (single-chain constructs) form.

39. (Previously Presented) The immunoconjugate according to claim 37, wherein said antibody is a murine, chimeric, humanized, or human monoclonal antibody, and said antibody is in intact, fragment (Fab, Fab', F(ab)2, F(ab')2), or sub-fragment (single-chain constructs) form.

40. (Previously Presented) The immunoconjugate according to claim 29, wherein said antibody is a monoclonal antibody that is reactive with an antigen or epitope of an antigen expressed on a cancer or malignant cell.

41. (Previously Presented) The immunoconjugate according to claim 40, wherein said cancer cell is a cell from a hematopoietic tumor, carcinoma, sarcoma, melanoma or a glial tumor.

42. (Previously Presented) The immunoconjugate according to claim 29, wherein said antibody is a monoclonal antibody that binds to an antigen selected from the group consisting of a B-cell lineage antigen, a T-cell antigen, a myeloid lineage antigen and a HLA-DR antigen.

43. (Previously Presented) The immunoconjugate according to claim 29, wherein said antibody is a monoclonal antibody that binds to an antigen selected from the group consisting of CD74, CD22, epithelial glycoprotein-1, MUC1, carcinoembryonic antigen (CEA or CD66e), colon-specific antigen-p, alpha-fetoprotein, CC49 antigen, prostate-specific membrane antigen, carbonic anhydrase IX, HER-2/neu, BrE3 antigen, CD19, CD20, CD21, CD23, CD33, CD45, CD74, CD80, VEGF, EGF receptor, PI GF, MUC2, MUC3, MUC4, gangliosides, HCG, EGP-2, CD37, HLA-DR, CD30, Ia, A3, A33 antigen, Ep-CAM, KS-1, Le(y), S100, PSA, tenascin, folate receptor, Thomas-Friedreich antigens, tumor necrosis antigens, tumor angiogenesis antigens, Ga

733, IL-2, IL-6, T101, MAGE, an antigen that binds to L243, CD66a (BGP), CD66b (CGM6) CD66c (NCA), CD66d (CGM1), TAC and combinations thereof.

44. (Currently Amended) The immunoconjugate according to claim 29, wherein said antibody is selected from the group consisting of LL2, L243, ~~MN-14~~, G250, J591, and CC49.

45. (Currently Amended) ~~The immunoconjugate according to claim 29, wherein~~

An immunocoujugate comprising:

(a) an antibody;

(b) a chemotherapeutic moiety; and

(c) a linker comprising (i) a thiol-reactive functional group that binds to a thiol group on the antibody, and (ii) a water-solubilizing moiety;

wherein said chemotherapeutic moiety is attached to said linker via an intracellularly-cleavable moiety that is cleavable by intracellular esterases and comprises an ester formed from the α -carboxylic acid of an amino acid;

said linker comprises a peptide comprising a thiol-reactive moiety at its N-terminus for linkage to the antibody and one or more side chain amino groups for linkage to at least one chemotherapeutic moiety;

and said antibody is a bispecific and/or bivalent antibody construct comprising one or more antibodies selected from the group consisting of LL2, L243, ~~MN-14~~, G250, J591, and CC49.

46-47. (Canceled)

48. (Previously Presented) The immunoconjugate according to claim 29, wherein said antibody links at least one chemotherapeutic moiety.

49. (Previously Presented) The immunoconjugate according to claim 48, wherein said antibody links to about 7 to 12 said chemotherapeutic moieties.

50. (Original) The immunoconjugate according to claim 30, wherein said functional group is a thiol-reactive or an amine-reactive group.

51. (Withdrawn) A method of treating a malignancy, an autoimmune disease, an infection, or an infectious lesion in a subject comprising administering to said subject a therapeutically effective amount of the immunoconjugate of claim 1.

52. (Withdrawn) The method according to claim 51, wherein said malignancy is a malignant solid tumor or hematopoietic neoplasm.

53. (Withdrawn) The method according to claim 51, wherein said immunoconjugate targets an antigen or epitope or iron-siderophore chelate receptor on a pathogen associated with said infection or infectious lesion.

54. (Withdrawn) The method according to claim 53, wherein said pathogen is selected from the group consisting of a bacterium, fungus, virus, rickettsia, mycoplasma and protozoa.

55. (Withdrawn) The method according to claim 53, wherein said pathogen is selected from the group consisting of Streptococcus agalactiae, Legionella pneumophilia, Streptococcus pyogenes, Escherichia coli, Neisseria gonorrhoeae, Neisseria meningitidis, Pneumococcus, Hemophilus influenzae B, Treponema pallidum, Lyme disease spirochetes, Pseudomonas aeruginosa, Mycobacterium leprae, Brucella abortus, mycobacterium tuberculosis, rabies virus, influenza virus, cytomegalovirus, herpes simplex virus I, herpes simplex virus II, human serum parvo-like virus, respiratory syncytial virus, varicella-zoster virus, hepatitis B virus, measles virus, adenovirus, human T-cell leukemia viruses, Epstein-Barr virus, murine leukemia virus, mumps virus, vesicular stomatitis virus, sindbis virus, lymphocytic choriomeningitis virus, wart virus, blue tongue virus, Sendai virus, feline leukemia virus, reo virus, polio virus, simian virus 40,

mouse mammary tumor virus, dengue virus, rubella virus, Plasmodium falciparum, Plasmodium vivax, Toxoplasma gondii, Trypanosoma rangeli, Trypanosoma cruzi, Trypanosoma rhodesiensei, Trypanosoma brucei, Schistosoma mansoni, Schistosoma japonicum, Babesia bovis, Elmeria tenella, Onchocerca volvulus, Leishmania tropica, Trichinella spiralis, Theileria parva, Taenia hydatigena, Taenia ovis, Taenia saginata, Echinococcus granulosus, Mesocestoides corti, Mycoplasma arthritidis, M hyorhinis, M. orale, M. arginini, Acholeplasma laidlawii, M. salivarium and M. pneumoniae.

56. (Withdrawn) The method according to claim 51, wherein said autoimmune disease is a class III autoimmune disease.

57. (Withdrawn) The method according to claim 56, wherein said class III autoimmune disease is selected from the group consisting of immune-mediated thrombocytopenias, dermatomyositis, Sjogren's syndrome, multiple sclerosis, Sydenham's chorea, myasthenia gravis, systemic lupus erythematosus, lupus nephritis, rheumatic fever, rheumatoid arthritis, polyglandular syndromes, bullous pemphigoid, diabetes mellitus, Henoch-Schonlein purpura, post-streptococcal nephritis, erythema nodosum, Takayasu's arteritis, Addison's disease, rheumatoid arthritis, sarcoidosis, ulcerative colitis, erythema multiforme, IgA nephropathy, polyarteritis nodosa, ankylosing spondylitis, Goodpasture's syndrome, thromboangiitis obliterans, primary biliary cirrhosis, Hashimoto's thyroiditis, thyrotoxicosis, scleroderma, chronic active hepatitis, polymyositis/dermatomyositis, polychondritis, pemphigus vulgaris, Wegener's granulomatosis, membranous nephropathy, amyotrophic lateral sclerosis, tabes dorsalis, giant cell arteritis/polymyalgia, pernicious anemia, rapidly progressive glomerulonephritis and fibrosing alveolitis.

58. (Withdrawn) The method of claim 51, wherein said immunoconjugate is administered parenterally.

59. (Withdrawn) The method of claim 51, wherein said targeting moiety is a monoclonal antibody that binds to an antigen selected from the group consisting of a B-cell lineage antigen, a T-cell antigen, a myeloid lineage antigen and a HLA-DR antigen.

60. (Withdrawn) The method according to claim 51, wherein said targeting moiety is a monoclonal antibody that binds to an antigen selected from the group consisting of CD74, CD22, epithelial glycoprotein-1, MUC1, carcinoembryonic antigen (CEA or CD66e), colon-specific antigen-p, alpha-fetoprotein, CC49 antigen, prostate-specific membrane antigen, carbonic anhydrase IX, HER-2/neu, BrE3 antigen, CD19, CD20, CD21, CD23, CD33, CD45, CD74, CD80, VEGF, EGF receptor, P1GF, MUC2, MUC3, MUC4, gangliosides, HCG, EGP-2, CD37, HLA-DR, CD30, Ia, A3, A33 antigen, Ep-CAM, KS-1, Le(y), S100, PSA, tenascin, folate receptor, Thomas-Friedreich antigens, tumor necrosis antigens, tumor angiogenesis antigens, Ga 733, IL-2, IL-6, T101, MAGE, an antigen that binds to L243, CD66a (BGP), CD66b (CGM6) CD66c (NCA), CD66d (CGM1), TAC and combinations thereof.

61. (Withdrawn) The method according to claim 51, wherein said targeting moiety is selected from the group consisting of LL1, LL2, hA20, 1F5, L243, RS7, PAM-4, MN-14, Mu-9, AFP-31, G250, J591, CC49 and Immu 31.

62. (Withdrawn) The method according to claim 51, wherein said targeting moiety is a bispecific and/or bivalent antibody construct comprising one or more antibodies selected from the group consisting of LL1, LL2, hA20, L243, RS7, PAM-4, MN-14, Mu-9, AFP-31, G250, J591, CC49 and Immu 31.

63. (Currently amended) The immunoconjugate according to claim 1, wherein said antibody is selected from the group consisting of LL1, hA20, RS7, PAM-4, Mu-9, and AFP-31, MN-14, hLL1, hRS7, hPAM4, and hMu9.

64. (Currently amended) The immunoconjugate according to claim 1, wherein said antibody is a bispecific and/or bivalent antibody construct comprising one or more antibodies selected from the

group consisting of LL1, hA20, RS7, PAM-4, Mu-9, and AFP-31, MN-14, hLL1, hRS7, hPAM4, and hMu9.

65. (Currently amended) The immunoconjugate according to claim 29, wherein said antibody is selected from the group consisting of LL1, hA20, RS7, PAM-4, Mu-9, and AFP-31, MN-14, hLL1, hRS7, hPAM4, and hMu9.

66. (Currently amended) The immunoconjugate according to claim 29, wherein said antibody is a bispecific and/or bivalent antibody construct comprising one or more antibodies selected from the group consisting of LL1, hA20, RS7, PAM-4, Mu-9, and AFP-31, MN-14, hLL1, hRS7, hPAM4, and hMu9.

67. (New) The immunoconjugate according to claim 1, wherein said antibody comprises the light chain variable region sequence comprising the CDR sequences KASQDVSIAVA (SEQ ID NO:7), SASYRYT ((SEQ ID NO:8) and QQHYITPLT (SEQ ID NO:9) and heavy chain variable region sequence comprising the CDR sequences NYGMN (SEQ ID NO:10), WINTYTGEPTYTDDFKG (SEQ ID NO:11) and GGFSSYWYFDV (SEQ ID NO:12).

68. (New) The immunoconjugate according to claim 1, wherein said antibody comprises the heavy chain variable region sequence comprising the CDR sequences NYGVN (SEQ ID NO:16), WINPNTGEPTFDDDFKG (SEQ ID NO:17), SRGKNEAWFAY (SEQ ID NO:18) and light chain variable region sequence comprising the CDR sequences RSSQSLVHRNGNTYLH (SEQ ID NO:13), TVSNRFS (SEQ ID NO:14) and SQSSHVPPT (SEQ ID NO:15).

69. (New) The immunoconjugate according to claim 1, wherein said antibody comprises the light chain variable region sequence comprising the CDR sequences RASSSVSYIH (SEQ ID NO:30), ATSNLAS (SEQ ID NO:31), QQWTSNPPT (SEQ ID NO:32) and heavy chain variable region sequence comprising the CDR sequences SYNMH (SEQ ID NO:33), AIYPNGDTSYNQKFKG (SEQ ID NO:34), STYYGGDWYFDV (SEQ ID NO:35).

70. (New) The immunoconjugate according to claim 1, wherein said antibody comprises the light chain variable region sequence comprising the CDR sequences SASSSVSSSYLY (SEQ ID NO:19), STSNLAS (SEQ ID NO:20) and HQWNRYPYT (SEQ ID NO:21) and heavy chain variable region sequence comprising the CDR sequences SYVLH (SEQ ID NO:22), YINPYNDGTQYNEKFKG (SEQ ID NO:23) and GFGGSYGFAY (SEQ ID NO:24).

71. (New) The immunoconjugate according to claim 1, wherein said antibody comprises the heavy chain variable region sequence comprising the CDR sequences EYVIT (SEQ ID NO:28), EIYPGSGSTSNEKFK (SEQ ID NO:29) and EDL, and light chain variable region sequence comprising the CDR sequences RSSQSIVHSNGNTYLE (SEQ ID NO:25), KVSNRFS (SEQ ID NO:26) and FQGSRVPYT (SEQ ID NO:27).

72. (New) The immunoconjugate according to claim 1, wherein said antibody comprises the heavy chain variable region sequence comprising the CDR sequences SYVIH (SEQ ID NO:1), YIHPYNGGTKYNEKFKG (SEQ ID NO:2) and SGGGDPFAY (SEQ ID NO:3) and light chain variable region sequence comprising the CDR sequences KASQDINKYIG (SEQ ID NO:4), YTSALLP (SEQ ID NO:5) and LQYDDLWT (SEQ ID NO:6).

73. (New) The immunoconjugate according to claim 1, wherein said antibody comprises the heavy chain variable region sequence comprising the CDR sequences TYWMS (SEQ ID NO:36), EIHPDSSTINYAPSLKD (SEQ ID NO:37) and LYFGFPWFAY (SEQ ID NO:38) and light chain variable region sequence comprising the CDR sequences KASQDVGTSVA (SEQ ID NO:39), WTSTRHT (SEQ ID NO:40) and QQYSLYRS (SEQ ID NO:41).